

§ 212.40

21 CFR Ch. I (4–1–16 Edition)

environmental conditions that could reasonably be expected to have an adverse effect on product quality.

(b) *Equipment procedures.* You must implement procedures to ensure that all equipment that could reasonably be expected to adversely affect the identity, strength, quality, or purity of a PET drug, or give erroneous or invalid test results when improperly used or maintained, is clean, suitable for its intended purposes, properly installed, maintained, and capable of repeatedly producing valid results. You must document your activities in accordance with these procedures.

(c) *Equipment construction and maintenance.* Equipment must be constructed and maintained so that surfaces that contact components, in-process materials, or PET drugs are not reactive, additive, or absorptive so as to alter the quality of PET drugs.

Subpart E—Control of Components, Containers, and Closures

§ 212.40 How must I control the components I use to produce PET drugs and the containers and closures I package them in?

(a) *Written procedures.* You must establish, maintain, and follow written procedures describing the receipt, login, identification, storage, handling, testing, and acceptance and/or rejection of components and drug product containers and closures. The procedures must be adequate to ensure that the components, containers, and closures are suitable for their intended use.

(b) *Written specifications.* You must establish appropriate written specifications for the identity, quality, and purity of components and for the identity and quality of drug product containers and closures.

(c) *Examination and testing.* Upon receipt, each lot of components and containers and closures must be uniquely identified and tested or examined to determine whether the lot complies with your specifications. You must not use in PET drug production any lot that does not meet its specifications, including any expiration date if applicable, or that has not yet received its

material release. Any incoming lot must be appropriately designated as quarantined, accepted, or rejected. You must use a reliable supplier as a source of each lot of each component, container, and closure.

(1)(i) If you conduct finished-product testing of a PET drug product that includes testing to ensure that the correct components have been used, you must determine that each lot of incoming components used in that PET drug product complies with written specifications by examining a certificate of analysis provided by the supplier. You are not required to perform a specific identity test on any of those components.

(ii) If you do not conduct finished-product testing of a PET drug product that ensures that the correct components have been used, you must conduct identity testing on each lot of a component that yields an active ingredient and each lot of an inactive ingredient used in that PET drug product. This testing must be conducted using tests that are specific to each component that yields an active ingredient and each inactive ingredient. For any other component, such as a solvent or reagent, that is not the subject of finished-product testing, you must determine that each lot complies with written specifications by examining a certificate of analysis provided by the supplier; if you use such a component to prepare an inactive ingredient on site, you must perform an identity test on the components used to make the inactive ingredient before the components are released for use. However, if you use as an inactive ingredient a product that is approved under section 505 of the act (21 U.S.C. 355) and is marketed as a finished drug product intended for intravenous administration, you need not perform a specific identity test on that ingredient.

(2) You must examine a representative sample of each lot of containers and closures for conformity to its written specifications. You must perform at least a visual identification of each lot of containers and closures.

(d) *Handling and storage.* You must handle and store components, containers, and closures in a manner that prevents contamination, mix-ups, and

deterioration and ensures that they are and remain suitable for their intended use.

(e) *Records.* You must keep a record for each shipment of each lot of components, containers, and closures that you receive. The record must include the identity and quantity of each shipment, the supplier's name and lot number, the date of receipt, the results of any testing performed, the disposition of rejected material, and the expiration date (where applicable).

Subpart F—Production and Process Controls

§ 212.50 What production and process controls must I have?

You must have adequate production and process controls to ensure the consistent production of a PET drug that meets the applicable standards of identity, strength, quality, and purity.

(a) *Written control procedures.* You must have written production and process control procedures to ensure and document that all key process parameters are controlled and that any deviations from the procedures are justified.

(b) *Master production and control records.* You must have master production and control records that document all steps in the PET drug production process. The master production and control records must include the following information:

(1) The name and strength of the PET drug;

(2) If applicable, the name and radioactivity or other measurement of each active pharmaceutical ingredient and each inactive ingredient per batch or per unit of radioactivity or other measurement of the drug product, and a statement of the total radioactivity or other measurement of any dosage unit;

(3) A complete list of components designated by names and codes sufficiently specific to indicate any special quality characteristic;

(4) Identification of all major pieces of equipment used in production;

(5) An accurate statement of the weight or measurement of each component, using the same weight system (metric, avoirdupois, or apothecary) for each component. Reasonable variations

are permitted in the amount of component necessary if they are specified in the master production and control records;

(6) A statement of action limits on radiochemical yield, i.e., the minimum percentage of yield beyond which investigation and corrective action are required;

(7) Complete production and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed; and

(8) A description of the PET drug product containers, closures, and packaging materials, including a specimen or copy of each label and all other labeling.

(c) *Batch production and control records.* Each time a batch of a PET drug is produced, a unique batch production and control record must be created. The batch production record must include the following information:

(1) Name and strength of the PET drug;

(2) Identification number or other unique identifier of the specific batch that was produced;

(3) The name and radioactivity or other measure of each active pharmaceutical ingredient and each inactive ingredient per batch or per unit of radioactivity or other measurement of the drug product;

(4) Each major production step (obtained from the approved appropriate master production and control record);

(5) Weights (or other measure of quantity) and identification codes of components;

(6) Dates of production steps and times of critical production steps;

(7) Identification of major pieces of equipment used in production of the batch;

(8) Testing results;

(9) Labeling;

(10) Initials or signatures of persons performing or checking each significant step in the operation; and

(11) Results of any investigations conducted.

(d) *Area and equipment checks.* The production area and all equipment in the production area must be checked to